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Specification and Drawings, as originally filed, with Application for Patent Serial No: **2,403,748**, on September 16, 2002, by **JOULE MICROSYSTMES CANADA INC.**, assignee of Peter R.H. McConnell and Bruce W. Adams, for "Optical System and Method of Analyzing Biological Tissue".

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OPTICAL SYSTEM AND METHOD OF ANALYZING BIOLOGICAL TISSUE

FIELD OF THE INVENTION

This invention relates to the field of optical detectors, in particular to spectrometers for medical purposes (eg. diseases and disorder detection) and research.

BACKGROUND OF THE INVENTION

Currently, clinical diagnosis of skin disease is generally accomplished by visual inspection under white light illumination. In this process, the reflectance light of a skin lesion is examined. Visual diagnosis alone may not be particularly accurate for early detection of skin cancer since many skin conditions have a similar appearance under white light. Therefore, when a suspect lesion is identified by visual examination, a biopsy is often performed for a definitive diagnosis. This is because it is crucial to diagnose skin pre-cancer or cancer at an early stage when it is curable. Thus, it is important to improve the clinical diagnosis of suspected skin lesions so as to avoid unnecessary skin biopsies.

Several approaches have been tried to improve dermatological diagnosis. Digital processing of reflectance images has been extensively investigated recently. Although reflectance imaging has led to improvements in the registration, recording, and documentation of skin lesions, there has been little improvement in the diagnostic accuracy. The foregoing approach does not provide any additional data to the physician making the visual assessment because it is still based on the reflectance pattern of a lesion under white light illumination, which is essentially the same pattern a human observer sees.

An alternative approach is ultraviolet (UV) or infrared (IR) photography that does extend visual perception of a physician to the UV or IR reflectance patterns. However, the

inconvenience due to delays in processing of film images renders this technique impractical for everyday use.

A further alternative approach that is already in widespread medical use involves a "Wood's lamp," which consists of a mercury discharge lamp associated with a filter that transmits UVA light with a 365 nanometer peak while absorbing visible light. When this device is used to assist in skin diagnosis, the eye serves as both the detector and the long pass filter. The eye is not sensitive to UV light, but is sensitive to visible fluorescence light when the "Wood's lamp" is used in a darkened room, where the physician sees an image of a fluorescing disease site. The "Wood's lamp" is useful for the diagnosis of some skin conditions such as tinea capitis, tinea versicolor, erythrasma, and some pseudomonas infections, as well as aiding in the detection and diagnosis of hypopigmented skin. It is of no value in conditions where the emitted fluorescence is not in the visible spectrum because the human eye cannot detect such fluorescence. It is also incapable of detecting Raman scattering. Thus, there has gone unmet a need for apparatus and methods that are able to detect and analyze fluorescence both within and beyond the visible spectrum, and that can use fluorescence, reflectance and/or Raman scattering to identify, and distinguish between, a variety of skin diseases.

There are a number of spectrophotometers for use in medical diagnosis. For example, U.S. Patent No. 6,069,689 describes an apparatus for diagnosis of a skin disease site using spectral analysis includes a light source for generating light to illuminate the disease site and a probe unit optically connected to the light source for exposing the disease site to light to generate fluorescence and reflectance light. The probe unit also collects the generated fluorescence and reflectance light and transmits this light to a spectrometer to be analyzed. The spectrometer generates and displays spectral measurements of the fluorescence light and the reflectance light, which in together assist the user in diagnosing the disease site. The apparatus makes use of a conventional personal computer using a plug-in spectrometer card to provide a compact and low cost system. The system performs combined fluorescence and reflectance spectral analysis in a quick and efficient manner to provide a powerful tool for dermatological diagnosis.

U.S. Patent No. 6,055,451 describes an apparatus and method that includes utilizing a device intended to be inserted into a patient's body to determine a characteristic of a target tissue. In one apparatus and method, a device illuminates the target tissue with amplitude modulated excitation electromagnetic radiation, and the device senses a returned electromagnetic radiation. A phase shift between the excitation and return electromagnetic radiation is determined, and the phase shift is used to determine characteristics of the target tissue. A demodulation factor, representing ratios of the AC and DC components of the excitation and return electromagnetic radiation may also be calculated and used to determine characteristics of the target tissue. In another apparatus and method embodying the invention, a device illuminates a target tissue with polarized electromagnetic radiation, and a return electromagnetic radiation is sensed. The amplitude of the returned electromagnetic radiation is sensed in mutually perpendicular planes, and this information is used to determine an anisotropy factor. The anisotropy factor, in turn, is used to determine characteristics of the target tissue. In either of the above-described methods, the return radiation could be a portion of the excitation radiation that has been reflected or scattered from the target tissue, or the returned electromagnetic radiation could be fluorescent emissions generated by endogenous or exogenous fluorophores located in the target tissue.

An apparatus and method for imaging diseases in tissue are presented in U.S. Patent No. 5,590,660. The apparatus employs a light source for producing excitation light to excite the tissue to generate autofluorescence light and for producing illumination light to generate reflected and back scattered light (remittance light) from the tissue. Optical sensors are used to receive the autofluorescence light and the remittance light to collect an autofluorescence light image and a remittance light image. A filter acts to integrate the autofluorescence image over a range of wavelengths in which the autofluorescence intensity for normal tissue is substantially different from the autofluorescence intensity for diseased tissue to establish an integrated autofluorescence image of the tissue. The remittance light image provides a background image to normalize the autofluorescence image to account for image non-uniformity due to changes in distance, angle and

illumination intensity. A monitor displays the integrated autofluorescence image and the remittance light image to produce a normalized image in which diseased tissue is distinguishable from normal tissue. The optical sensor can be installed adjacent the end of an endoscope probe inserted into a body cavity. A method for imaging diseased tissue using an integrated fluorescence image and a normalizing remittance image is also disclosed.

SUMMARY OF THE INVENTION

This invention provides an optical system comprising a spectrometer, an electronic light modulator and digital signal processing means, including: a) a photonic energy source which is controlled by said digital signal processing means to emit electromagnetic radiation which can range from ultraviolet to far infrared (or bandwidth from 150 to 3000 nm); b) an illumination monochromator which is controlled by said digital signal processing means to receive light from an illumination device and to deliver one or more wavelengths; c) an optical probe, which delivers light at one or more wavelengths to a subject area, located in an assembly that orients the illumination optics with that of the collecting means for gathering and delivering the resultant radiation to the detection monochromator; d) a receiving monochromator which is controlled by said digital signal processing means to perform specific digital signal processing tasks to pass the one or more wavelengths' reactive characteristics at a specific time; e) a photodetector device to sense the radiation at a specific time; and f) a digital signal processing means to perform the match filtering on the output of the photodetector.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a schematic diagram of the system components corresponding to one embodiment of the present invention.

Figure 2 is a schematic diagram of the diagnostic system according to one embodiment of the present invention comprising a spectrometer incorporating a Matched Filter Receiver, a Central Processing Unit,

Figure 3 is a schematic diagram of a scanning spectrometer system according to a further embodiment of the present invention incorporating a Matched Filter Receiver.

Figure 4 is a schematic diagram of a digital signal processing light pulse processing algorithm.

Figure 5 is an example of a 3-D Surface plot.

Figure 6 demonstrates On-Off keyed signal with a 0 dB signal to noise ratio, using pulse amplitude modulation detection.

Figure 7 demonstrates signal detection using frequency domain detection.

Figure 8 demonstrates the results of the time domain correlation output from binary pulse coding signal detection.

Figure 9 is a schematic representation of a pulse coding channel model.

Figure 10 depicts the detector output using a linear FM Chirp, which is a 125 msec wide rect function, swept from 500 Hz to 3500 Hz and sampled at 8000 samples/sec.

Figure 11 demonstrates the use of a linear FM pulse coding technique where the pulse duration was left at 0.125 seconds and the bandwidth was 1600 Hz for a time bandwidth product (TBP) of 200. A log scale of the detector was calculated as; $P = 20 \times \log s$, where s is the time domain output of the matched filter.

Figure 12 demonstrates the use of a linear FM pulse coding technique as in Figure 11 for a TBP of 800.

Figure 13 demonstrates the use of a linear FM pulse coding technique as in Figure 11 for a TBP of 2250.

Figure 14 is a time domain plot for the case of a TBP of 2250, where the detector amplitude was plotted.

Figure 15 is a schematic representation of a spectrometer that incorporates a matched filter receiver.

Figure 16 shows a detector output, recorded for λ_i and λ_e, from the spectrometer of Figure 15 and plotted for display.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

The term, electronic light modulator, means an acousto-optic modulator, mechanical light chopper, hologram, and electrically driven opto-electonics.

The term, an illumination light source, means a light emitting diode (LED), incandescent, laser, gas discharge lamp, laser diode, arc lamp, x-ray source.

The term, monochromator, refers an interference filter, cutoff filter, diffraction prism, diffraction grating, interferometer, hologram.

The term, collecting means, includes diffraction or reflective optics, lenses, mirrors, or optical fibres.

The term, photodetector device, includes photodiode, photomultiplier, charge couple device (CCD).

The phrase, an analog circuit to condition the signal from the photodetector, includes amplifier, DC Level shifter, gain control, and noise prefiltering.

The term, coding signal, includes amplitude modulated, phase modulated, frequency modulated, and phase and amplitude modulated signal.

The term, resultant radiation, refers to each or all of the reflected, transmitted, absorbed and fluoresced light that result when a subject is exposed to an illuminating radiation.

The phrase, weak signal detection, refers to techniques used to enable measurement of low intensity emission radiation from a sample. For any given signal to noise ratio, increasing the bandwidth used to transfer the information can lower the information error rate. The signal bandwidth is spread prior to transmission in the noisy channel, and then despread upon reception. This process results in what is called Processing Gain.

The term, signal spreading, refers to a number of means of spreading the signal, including Linear Frequency Modulation (sometimes called Chirp Modulation) and Direct Sequence methods.

The term, signal despreading, refers to a process, which is accomplished by correlating the received signal with a similar local reference signal using a Correlation Receiver or Matched Filter receiver technique. When the two signals are matched, the spread signal is collapsed to its original bandwidth before spreading, whereas any unmatched signal is spread by the local reference to essentially the transmission bandwidth. This filter then rejects all but desired signal. Thus, in order to optimize a desired signal within its interference (thermal noise in the detection system, ambient light induced noise, AC line noise, etc.), a matched filter receiver enhances the signal while suppressing the effects of all other inputs, including noise.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

The various aspects of this invention will become more readily appreciated and better understood by reference to the following detailed description.

The system comprises a scanning spectrometer incorporating an electronic light modulator, and digital signal processing means. The spectrometer technique combined with optical signal encoding provides the ability to obtain spectral signatures of a sample, enabling one to perform many functions on a scanned sample such as biological tissue. One example of tissue scanning includes techniques such as identification of diseased tissues, (eg. cancerous tissue) and delineation between diseased and healthy tissue. Because of the enhanced signal-to-noise ratio provided by this system, this invention can detect changes in diseased tissue that are more subtle than would be possible with currently available optical systems.

With reference to Figure 1, the optical system of the present invention comprises a spectrometer and a digital signal processing means **5**, comprising: a photonic energy source **15** which is controlled by said digital signal processing means **5** (specifically the emitter control electronics **10**), to emit electromagnetic radiation which can range from ultraviolet to far infrared (or bandwidth from 150 to 3000 nm); optical emission processing means **20** which is controlled by said digital signal processing means **5** (specifically the emitter control electronics **10**) to receive light from the photonic energy source **15** and to deliver one or more illumination wavelengths in a pulse sequence to a test sample **25**, wherein the optical emission processing means **20** can comprise a means for isolating one or more illumination wavelengths and emitter optics that orient and focus the illumination wavelength(s) onto the test sample **25**; received light optical processing means **30** which is controlled by said digital signal processing means **5** (specifically the emitter control electronics **10**) to collect and isolate one or more

wavelengths of received light due to the illumination of a test sample **25**, wherein the received light optical processing means **30** can comprise detector optics for collecting the received light from the test sample 25 and a means for isolating one or more of the wavelengths of the received light; an optical detector **35** to sense and convert to an electrical signal the received light which has been transmitted by the received light optical processing means **30**; and a DSP received signal processing means **40**, which is a component of the digital signal processing means **5**, to perform the match filtering on the output of the optical detector **35**, wherein said match filtering is performed based on the received electrical signals from the optical detector **35** and control parameters from the emitter control electronics **10**.

In one embodiment of the present invention, the optical system further comprises a database of spectral characteristics of a plurality of tissue samples, for example, which may include a plurality of healthy states and a number of disease states of tissue or any other material that can be identified by a spectral analysis. This database provides a means for identifying a test sample based on its spectral characteristics by correlating the spectral characteristics of the test sample with the spectral characteristics of a plurality known samples based maintained in the database.

In one embodiment of the present invention the optical system comprises a spectrometer, an electronic light modulator and digital signal processing means, comprising: a) a photonic energy source which is controlled by said digital signal processing means to emit electromagnetic radiation which can range from ultraviolet to far infrared (or bandwidth from 150 to 3000 nm); b) an illumination monochromator which is controlled by said digital signal processing means to receive light from a photonic energy source and to deliver one or more wavelengths in a pulse sequence; c) an optical probe, which delivers light at one or more wavelengths to a subject area, located in an assembly that orients the illumination optics with that of the collecting means for gathering and delivering the resultant radiation to the detection monochromator; d) a receiving monochromator source which is controlled by said digital signal processing means to perform specific digital signal processing tasks to pass the one or more wavelengths'

reactive characteristics at a specific time; e) a photodetector device to sense the radiation at a specific time; and f) a digital signal processing means to perform the match filtering on the output of the photodetector.

There are various locations for noise or interference to enter the system according to the present invention, with this interference decreasing the ability to detect signals received from the test sample due to its illumination. For example and with further reference to Figure 1, ambient light can enter the system through the received light optical processing means **30** and electrical noise can enter the system through the DSP received signal processing means **40**. The incorporation of a digital signal processing means can provide a means for the encoding of the illumination signal and the matched filtering of the received signal in relation to the encoded illumination signal, and as such can provide improved detection of the received signals resulting from the illumination of the test sample.

There are a number of embodiments of this optical system, comprising different components. Each embodiment, however, has a form of each of these components. Some criteria for choosing which component should be included in a particular embodiment will be described below.

In order to describe how the components operate together, an overview of one embodiment of the system of the present invention is presented in Figure 2, depicting an optical system comprising a spectrometer with an electronic light modulator and digital signal processing means. In this embodiment an illumination light source **100** is controlled by digital signal processing means **300** to emit a radiation bandwidth ranging from, for example, 250 to 1000 nanometers. The light modulator **200** which could be an encoding disc (as shown in Figure 1), acousto-optic modulator, or electronic modulator such that might provide Amplitude or Phase modulation, essentially spreads the optical signal, which in this embodiment is a single bit of information (the illumination scan). An illumination monochromator **120** is controlled by digital signal processing means **300** to receive light from the illumination light source **100** and to deliver the N^{th} wavelength in a

pulse sequence. An optical probe delivers the N^{th} wavelength to a subject area **140**, for example, tissue. The resultant radiation is collected and delivered to the emission monochromator **160**. Radiation signals detected from the subject are still encoded with the spread function coding and the intensity is proportional to the reflection coefficient and the fluorescence coefficient respectively. The detection monochromator **160**, which is controlled by digital signal processing means **300**, separates the reflection and fluorescence spectra optically, by performing specific digital specific processing tasks to pass the N^{th} wavelength reactive characteristics at a specific so that each of these encoded optical signals can be detected by the photo detector **170**. The photo detector **170** detects the weak optical signal and converts it to an electrical signal, which is then processed by the bandpass filter **180**, (essentially an Analog to Digital Converter) and transmits it to the digital signal processing means **300**. If the time domain spreading function is represented by $F(\omega)$ and the received signal is represented by $H(\omega)$, then the output of the matched filter receiver is obtained using the digital signal processor:

$$S(t) = \int F(\omega)H(\omega)e^{j\omega t}d\omega$$

Since a matched filter receiver is a linear system, $s(t)$ is directly proportional to the intensity of the reflectance and fluorescence illumination on the detector.

A Spectrometer

In one embodiment of the present invention, the optical system comprises a spectrometer, an electronic light modulator and digital signal processing means. For an optical system to be used to identify the parameters of reflectance, fluorescence and absorption there must be known qualities of all the spectral characteristics across a broadband spectrum that defines the subject vs. any similar subject. The optical properties, in conjunction with the signal processing properties of the device, give it the ability to isolate the properties of subjects by a method that creates a matrix of specificity (by selective wavelength and spectral resolution) and sensitivity (irradiance).

In one embodiment of the present invention, the optical spectrometer consists of a dual optical system with one monochromator electronically controlled to select the

illumination wavelength and a second monochromator electronically controlled to select the reflectance and fluorescence emission wavelengths from the sample in the area of interest.

In one embodiment, the requirements of the spectrometer are that: 1) it is able to resolve optical spectra over the range 250 nm to 800 nm; 2) the spectral resolution is on the order of 5 nm of better; and 3) that it has a stray light suppression of 10^{-5} or better, for both the illumination and emission units.

A spectral resolution of 5 to 10 nm can allow reasonable sampling of the fluorescence peaks, which appear to be the order of 30 to 50 nm. Finer resolution may be useful in some applications.

In choosing the illumination wavelength, the factors that should be balanced are overall scanning time for the area of interest and the resolution of the scan. The total number of steps N required to sweep out the emission and fluorescence spectrum is;

$$N = n_i \cdot n_d/2$$

where:

n_i = number of steps for the illumination monochromator

n_d = number of steps for the reflection/fluorescence monochromator

The factor 1/2 determines that only the diagonal terms of the emission/fluorescence matrix are of interest and terms on one side of the diagonal. Moreover, N is proportional to $\Delta\lambda/2$, where $\Delta\lambda$ is the spectral resolution of a monochromator. Since the scanning time is proportional to N, then there is a trade-off between $\Delta\lambda$ and the scanning time.

The stray light suppression factor required depends on how small an area of fluorescence one wishes to detect. Stray light essentially determines the optical noise floor for the system, and sets the limit of optical detectability.

A Photonic Energy Source

Each embodiment includes a photonic energy source, which is controlled by said digital signal processing means to emit electromagnetic radiation, which can range from ultraviolet to far infrared (or bandwidth from 150 to 3000 nm).

A photonic energy source which can be used in conjunction with the present invention can be selected from the group comprising: a laser, laser diode, light emitting diode (LED), arc flashlamp or a continuous wave bulb. The selection of the photonic energy source to be used in a particular embodiment of the present invention can be determined by the required spectral analysis. The functionality of the device may require a broad spectral analysis of a test sample or may require the spectral characteristics over a narrow bandwidth or even specific wavelength, for example.

For example, a laser has a very narrow spectrum (a highly coherent "single" wavelength), narrow spatial beam, and high pulsed power. An incandescent light bulb has a broad spectrum, wide beam, and continuous transmission.

In one embodiment of the present invention, the electromagnetic radiation generated by the photonic energy source may be in the form of pulsed electromagnetic radiation.

Optical Emission Processing Means

The optical emission processing means receives light from the photonic energy source and delivers one or more illumination wavelengths in a pulse sequence to a test sample, wherein the optical emission processing means can comprise a means for isolating one or more illumination wavelengths and emitter optics that orient and focus the illumination wavelength(s) onto the test sample. The optical emission processing means is controlled by the emitter control electronics contained in the digital signal processing means, wherein the emitter control electronics may perform functions comprising pulse coding and pulse shaping.

In order to distinguish the light wavelengths of reflection and fluorescence, which are received from the test sample, from ambient light noise, the illumination of the test sample should be performed using narrowband illumination, for example, a laser is a narrowband light source.

In one embodiment of the present invention a generic device may require the ability to easily vary the emission spectral characteristics, such that spectral characteristics of the test sample can be determined for a range of illumination wavelengths. This can be accomplished by using a broadband light source, such as a halogen bulb or a Xenon tube and subsequently using wavelength separation optics to filter the emitted light thereby isolating narrow portions of the spectrum for illuminating the test sample. An alternate approach is to use an array of multiple narrowband or mediumband light sources (eg. laser diodes and/or various coloured LED's), each having particular desired spectral characteristics, and subsequently activate them one at a time, which effectively traverses a broad spectrum of light and isolates particular illumination wavelengths during the sequence of illumination of these devices.

The optical control processing means further comprises a light control device, which provides a means for modulating the light, which is to illuminate the test sample, for example producing a pulsed sequence of light emission. A light control device can be an indirect light modulator, for example, a light chopper, shutter, liquid crystal filter, galvanometric scanner or acousto-optic device. In addition, light modulation can be performed in a direct manner using an amplitude modulator circuit or a frequency modulator circuit.

The wavelength separation optics can be selected from fixed light conditioning optics including optical filters, refractive optics and diffractive optics and a variable light conditioning subsystem including a refractive or diffractive optical system whereby the optical centre wavelength is chosen by the use of a position controlled reflective surface after the light has passed fixed light conditioning optics or a refractive or diffractive optical system whereby the optical centre wavelength is chosen by use of a position

controller to move fixed light conditioning optics. An example of a wavelength separation optic device is a monochromator.

Emitter optics can be used to transmit the photonic energy between the components of the optical emission means and also to transmit the illumination light to the test sample. The emitter optics can be selected from the group comprising, condensers, focusing devices, fibre optics and apertures.

In one embodiment of the present invention, the optical system can include two monochromators: one monochromator which is controlled by said digital signal processing means to receive light from the illumination device and to deliver one or more wavelengths in a pulse sequence and a second a monochromator source which is controlled by said digital signal processing means to perform specific digital specific processing tasks to pass the one or more wavelengths' reactive characteristics at a specific time.

In one embodiment of the present invention, the optical system includes an optical probe, which delivers light at one or more wavelengths to a subject area, located in an assembly that orients the illumination optics with that of the collecting means for gathering and delivering the resultant radiation to the detection monochromator, for example.

Received Light Optical Processing Means

The received light optical processing means collects and isolates one or more wavelengths of received light from the test sample, with this received light being related to the illumination of the test sample as described above. The received light optical processing means can comprise detector optics for collecting the received light from the test sample and a means for isolating one or more of the wavelengths of the received light for detection by the optical detector. The received light optical processing means is controlled by the emitter control electronics contained in the digital signal processing means and thus its function can be correlated with the optical emission processing means, which can provide a means for the efficient analysis of the received spectral emissions.

In one embodiment of the present invention, the received light optical processing means can isolate particular wavelengths of received light by using wavelength separation optics, which provides a means for isolating one or more wavelengths of received light thus allowing the received light to be correlated to the illumination wavelength.

The wavelength separation optics can be selected from fixed light conditioning optics including optical filters, refractive optics and diffractive optics and a variable light conditioning subsystem including a refractive or diffractive optical system whereby the optical centre wavelength is chosen by the use of a position controlled reflective surface after the light has passed fixed light conditioning optics or a refractive or diffractive optical system whereby the optical centre wavelength is chosen by use of a position controller to move fixed light conditioning optics. An example of a wavelength separation optic device is a monochromator.

In a further embodiment of the present invention, the received optical processing means may be required to isolate one selected wavelength, for example, if the test specimen is illuminated by a particular wavelength of light and the reflection of this photonic energy by the test sample is required, the received optical processing means can have a fixed light separation means, since only a particular light wavelength is being evaluated.

Detector optics can be used to transmit the photonic energy between the components of the received light optical processing means and also to transmit the received light to the optical detector. The detector optics can be selected from the group comprising, condensers, focusing devices, fibre optics and apertures.

Optical Detector

Each embodiment includes an optical detector which can sense the light transmitted by the received light optical processing means and convert this into an electrical signal for processing by the digital signal processing means and in particular the DSP received

signal processing means incorporating information from the emitter control electronics, for example, pulse timing.

An optical detector can be a diode, photomultiplier, or a charge-coupled device (CCD) arranged in a linear array or an area array, for example. A specific example is a blue enhanced Gallium-Arsenide photodiode.

An Analog Circuit

In one embodiment of the present invention, the optical system includes an analog circuit to condition the signal from the photodetector.

One example of a signal processing system involves both analog front-end and digital back-end tasks. In general the analog processing tasks are concerned with recovering the small sensor signals and applying highly selective filtering operations. The digital domain tasks are concerned with further signal filtering as well as analysis functions, in relation to energy detection and data output.

To minimize the interference and to provide immunity against shot noise, the illumination signal is modulated by a frequency of typically a few hundred Hz. The analog section is designed to high gain amplify and prefilter the photodiode output and recover the modulation frequency. Utilizing these signals, a narrowband tracking filter can provide the very high selectivity for modulated signal recovery.

The output of the narrowband filter, after amplification, is analog/digital converted and input into a DSP (digital signal processor) which in real time performs the back-end tasks of filtering, energy detection, averaging and converting the results into usable data. The filtering will further enhance the rejection of a/c noise and harmonic distortion, which may have been introduced in the final stages of analog processing. The filtering is followed by an averaging energy detector, which outputs the values proportional to the energy of the sensor signal. These values are sent to the host computer in short intervals, where they can be stored and processed for further analysis.

The utilization of advanced signal processing techniques, enables the detection of optical reflectance and fluorescence emissions that would normally not be able to be detected

Moreover, the signal processing algorithms can be implemented in standard Digital Signal Processing chips, enabling the overall cost of devices based on this technology to be relatively low. The economical cost factor allows for devices to be used with patients who would not normally gain access to such diagnostic tools.

Digital Signal Processing Means

Digital Signal Processing (DSP) means can be used to control the photonic energy source, the optical emission processing means and the received light optical processing means in order to be able to detect one or more wavelengths of the resultant radiation in relation to one or more wavelengths of illumination radiation. The digital signal processing means comprises emitter control electronics, which provide a means for controlling the illumination radiation and the received light. In addition, the DSP means comprises a received signal processing means which enables the DSP to correlate the received light radiation with the illumination radiation, which can provide a means for identifying reflectance, fluorescence and absorption from a test sample due to its illumination. The DSP can be incorporated into a computer system in the form of a circuit board which is installed in a computer which can provide a means for manipulating the received radiation after matched filtering or the DSP may comprise stand alone hardware providing a means for DSP to function independently.

The emitter control electronics which control the illumination radiation performs tasks including: supplying electrical power and driving circuitry to convert electrical to light energy, controlling the amplitude and timing of light source pulses, controlling optical devices which filter, focus, or mechanically pulse the illumination radiation, for example, light filters, monochromator, collimator, chopper. In addition, the emitter control electronics provide a means for controlling the received light optical processing means enabling the isolation of reflectance and fluorescence light wavelengths from the test

sample due to its illumination. For example, the incorporation of a monochromator into the received light optical processing means can provide a means for isolating the desired wavelengths.

The coding function of the emitter control electronics can be provided by means selected from the group comprising: pulse code software to create synchronous pulse for direct modulation of the light control device frequency (PFM), pulse code software to create synchronous pulse for direct modulation of the light control device amplitude (PFA), pulse code software to create synchronous pulse for direct modulation of the light control device pulse width (PFW), a function generator to create a fixed synchronous pulse for pulse rate and amplitude modulation and a mechanical encoder driver to create a synchronous pulse for an indirect light modulator, for example a chopper, shutter, galvomirror etc.

The DSP received signal processing means enables matched filter correlation between electrical signals received from the optical detector and the corresponding time period as defined by the emission control electronics. This correlation between transmitted and received signals can provide a means for enhanced identification of received signals over the noise (ambient light or electrical for example) which enters into the system of the present invention. Filtering and time averaging of received signals, synchronized and matched with the emitted pulse sequence, enhances the signal-to-noise ratio (SNR) and improves the confidence in the measurement of the sample response at the wavelength of interest.

A matched filter is an exact copy of the signal of interest. The filter is correlated with the input signal, with this procedure basically being a sum of the products of the signal multiplied by the filter over the total duration of the filter. Upon the matching of the filter and the signal of interest, the correlation (convolution) sum typically peaks relative to the non-matched sums providing a means for identifying the signal over the external noise within the optical system. In one embodiment of the present invention, a bank of narrowband filters centered at intervals of the pulse rate can capture more lines from the

pulse spectrum, and thus may provide a means for improved light pulse energy estimation and subsequent identification of the detected wavelength.

In one embodiment of the present invention, the digital signal processing means can be designed as illustrated in Figure 4. The pulses generated by the photodetector as a result of photonic radiation detection are transmitted to an analog low pass filter (LPF) **400**, which transmits the filtered information to a analog to digital converter (ADC) **410**. The analog LPF can suppress frequencies over 10 kHz, for example, for anti-aliasing. This digitized information is sent to a bank of narrowband finite impulse response (FIR) filters **420**, wherein each filter is matched to one of the lines in the pulse sequence spectrum (input signal pulse). This provides a means for matching the pulse spectrum in order to identify the signal over the external noise within the system (match filtering). The sums of the filter - input signal correlation **430** are transmitted to the peak detector though pulse period buffers **440** and **480** and the average light measured is then sent to the control logic **500** of the DSP. The measured light signals are subsequently transmitted to a computing device located on a personal computer, for example, via a RS232 serial port **510**. The control logic **500** provides a means to perform scheduling control and configuration control of the digital signal processing (DSP) means. In addition to the post detection filtering performed by the DSP, a pulse sequence generator **450** transmits a pulse period counter to the pulse period buffer **440** and further transmits a digital signal defining the generated sequence to a digital to analog converter **460**. The resulting analog Pulses are sent to the light source upon passing through an analog low pass filter **470**.

Weak Signal Detection

In one embodiment, the tone encoded method is used for signal encoding due to its basic simplicity, and the fact that it yields a reasonable degree of noise suppression relative to the complexity. In this embodiment, the key consideration is the amount of time required to take one measurement. This is determined by: 1) the amount of time required to acquire the samples for a frequency domain transfer, which is essentially number of samples required divided by the sample rate; and 2) the filter bandwidth in the case of a

bandpass filter technique, which is essentially the reciprocal of the bandwidth of the filter.

The trade-off with the electrical signal bandwidth is observation time versus noise. As the bandwidth is increased and the observation time decreased, the noise power increases in proportion to the bandwidth. Any increase in noise reduces the detector sensitivity. The total processing time to scan the area of interest is simply $T = N\tau$, where τ is the time for one measurement at one wavelength. The two key variables in the observation time are the optical filter bandwidth and the electrical filter bandwidth.

A rough first order calculation of T can be made by making the following assumptions: 1) resolve optical spectra over the range 250 nm to 800 nm; 2) use an optical resolution bandwidth of 10 nm; and 3) use an electrical bandpass filter BW of 10 Hz, therefore $\tau =$ 0.10 sec. By using these assumptions, the scanning time is 151.25 seconds, or about 2.5 minutes.

When a subject to be examined is exposed to illuminating radiation, the detection of reactive radiation characteristics is the goal. In general, the fluorescent light will be much weaker than the reflected light. The spectral resolution required is determined by the ability of the optical spectrometer system to discriminate between reflected and fluorescent wavelengths. This is achieved through the use of a prism and/or grating monochromators with variable apertures, which suppress stray radiation.

For optical signatures to be adequately resolved, the system must be able to detect very weak electrical signals, which result from the optical radiation being detected by the photodiode. Ultimately, the goal is to detect a very weak signal in a background of noise due to electrical noise, optical background radiation, and out of band emissions from the subject (due to the spectrometer spectral resolution).

Other variables in the measurement of spectral signatures comprise: a) time duration the subject is illuminated; b) the amplitude of the illumination at the subject first surface; c)

the amplitude of the noise variables; d) spectral shifts in the illuminators over time; and e) the decay of the fluorescence emitted by a test sample after the illumination of the test sample has been discontinued. These variables need to be addressed to compare the performance of various detection schemes.

In one embodiment of the present invention, adaptive filtering of the received light may enable the detection of the decaying intensity of fluorescence emitted from a test sample upon the discontinuation of the illumination of the test sample. The discontinuation of the illumination may be complete termination of transmission of photonic energy or the discontinuation of a particular illumination wavelength. The measurement of the decay of fluorescence emitted by a test sample using a device according to the present invention may provide a means for the identification of a test sample.

Pulse amplitude modulation techniques as applied to this situation are essentially On-Off keying of the illumination. The detection is based on the ability to detect the presence of the signal in an ambient noise. The signal detectability depends on the ability to discriminate the signal from the noise, and generally requires a signal power much greater than the noise (> 10 dB typically). An example of an On-Off keyed signal is shown in Figure 6. The signal to noise ratio (SNR) in this case is 0 dB, and it is not possible to distinguish the noise portion of the signal from that consisting of signal plus noise.

The frequency domain detection mechanism is simply a detection means based on frequency modulation of the signal with a constant frequency modulation. This has great advantages over time domain detection means such as On-Off keying. Even though the RMS amplitudes of the signal and the noise can be equal (SNR = 0 dB), the power spectral density of the modulated signal is usually much greater than the power spectral density of the broadband noise. The carrier can be isolated from the noise by a number of means, including: a) spectral measurement techniques, such as a DFT or FFT; and b) narrow band filtering with the centre frequency of the filter located at the modulation frequency.

An example of this is shown in Figure 7. In this case, the RMS amplitudes of the first signal and the noise are equal (SNR = 0 dB). Two other signals were added which had magnitudes relative to the first signal of 0.50 and 0.1 respectively. The time domain signal happens to look exactly like that shown in Figure 6. In the frequency domain however, the spectral peaks for the first and second signals are very apparent. The spectral signature for this signal is buried in the noise and cannot be resolved. This detection technique is relatively simple to implement in practice, and is suitable for use in the optical spectrometer.

The pulse coding techniques (binary, linear, enhanced) are an alternative means of detection. Pulse coding techniques are often used to detect very weak signals in the presence of noise. They are more complex than traditional techniques such as tone detection and pulse amplitude detection, however they are sometime the only choice when amplitude of the signal to be detected is weak relative to the noise and there are no means available to increase the signal to noise ratio other than pulse coding. Two exemplary pulse coding techniques are Binary Pulse Coding and Linear Frequency Modulation (FM) Coding. Both of these techniques fall into the realm of pulse compression and spread spectrum, and they are adequately described in numerous references (Barton, DK (1978) Radars Volume 3: Pulse Compression, Artech House Inc.).

Binary Pulse Coding, as an example, uses a 1000-bit synchword, which can be created, by using a uniform random number generator and constructing a binary sequence from that data. Pulse are generated at specific locations in the time domain and the relative amplitudes are measured. Results of a time domain correlation output are shown in Figure 8. In an amplitude plot, all three pulses can be detected. The third and smallest signal pulse is just distinguishable from the noise.

Linear FM Pulse Compression schemes have traditionally been used in radar systems to reduce the overall peak power of transmitted signal while still achieving large detection

ranges. They also figure prominently in Synthetic Aperture Radar processing for airborne and spaceborne imaging radars. This form of coding is achieved by linearly sweeping a carrier signal from f_1 to f_2 (for a swept bandwidth of Δf) for a duration τ. In general, the "*output power*" of a linear FM coded signal is increased by the Time Bandwidth Product (TBP) $\Delta f\tau$, which is the product of the pulse duration in seconds and the swept bandwidth in Hertz. The detection process is essentially a matched filter detector, which is matched to the linear FM transmitted pulse. The overall process is shown in Figure 9. The signal s(t) is usually a *Dirac Delta function*, which in reality is simply the trigger pulse for the encoder h(t) which generates the transmitted signal $U(\tau,\Delta f)$ which is the linear FM coded pulse (or Chirp) which has a duration τ and a bandwidth Δf. This is the signal that would drive an optical emitter to illuminate a subject. Noise n(t) is added to the coded signal in both the optics and the electronics. This optical signal is detected by a photo detector, whose electrical output signal is comprised of the actual optical signal of interest, optical background noise, and electrical noise in the photo detector and electronics. The matched filter detector then processes this electrical signal. Since the optical signal of interest is the only one of the three components of the signal, which is matched to the matched filter, it is the only component which experiences gain due to the linear FM pulse coding. The optical and electrical noise components are essentially suppressed relative to the coded signal. This is the key advantage of such a scheme. A linear FM Chirp output is shown in Figure 10. In the amplitude plot, only the largest two pulses can be detected, with the third being buried in the noise and it is arguable if it is visible or not. This example graphically demonstrates the coding gain offered by a linear FM Pulse Compression Technique.

Enhanced Pulse Coding Techniques take advantage of the fact by increasing the Time Bandwidth Product, greater coding gain can be achieved. Using this technique the weakest of the time domain pulses was just visible.

A plot of the original case with a TBP of 200 is shown in Figure 11 and the new case with a TBP of 800 is shown in Figure 12. The increase of the time bandwidth product has increased the coding gain sufficiently enough that the third and weakest pulse is now

visible above the noise floor (just). The coding gain was increased from 23.0 dB to 29.0 dB, or an overall increase 6.0 dB. In both plots, the power has been normalised to the peak located at sample 100. The drop in the noise floor in going from a TBP of 200 to 800 is readily apparent.

To further make this point, plot for the case of a TBP of 2250 is shown in Figure 13. In order to compare this high time bandwidth product detection scheme to the other coding techniques, a time domain magnitude plot where the detector amplitude has been plotted is shown in Figure 14. The noise amplitude should be suppressed by $\sqrt{2250}$, or about 47.4. The peak amplitude of pulse 1 is 2505, pulse 2 is 1252, and pulse 3 is 250. The noise magnitude was the same as that for the signal for peak 1, therefore the noise magnitude should be suppressed to a level of approximately 52. As seen from Figure 14, this is, more or less, the case. Due to the high level of noise suppression achieved, the signal for pulse 3 is quite visible relative to the noise background. This is readily apparent when the TBP=375 case in Figure 10 where pulse 3 is not visible is compared with the TBP = 2250 case in Figure 14 where pulse 3 is readily visible.

Higher Time Bandwidth Products can be used to achieve higher coding gains, however these may be limited depending on the means used to achieve the signal coding. A mechanical chopper would be limited by the ability to replicate the linear FM code onto the chopper wheel, whereas acoustic-optic modulators could achieve much higher TBP's but at much higher expense.

Scanning Methodologies

For manual scanning, the probe is moved manually across the surface to be analyzed, and analyzes only the area immediately under observation. The spectral characteristics are observed at a fixed point in space (x_o, y_o). Thus, one obtains a one-dimensional plot of the spectral response for each point (x_o, y_o). This mode of operation is useful if the fluorescing material is diffusely distributed throughout the medium to be observed, or if localized analysis is required.

For two-dimensional scanning, the probed is moved (or scanned in some other manner) across a two dimensional surface and spectral responses are obtained for each point (x_i, y_i, λ) in the plane. This method represents an analysis of a sample in three dimensions, that is (x_i, y_i, λ). This mode of operation is useful if the fluorescing material is highly localized within a larger area of observation.

For three-dimensional scanning, quantitative and qualitative data can be obtained for closed loop feedback control and detection of physical and optical characteristics in subject matter. As the probe is scanned across a two-dimensional surface, spectral responses are obtained for each point (x_i, y_i, z_i, λ).

An Automated Tissue Type Classification Scheme

The system and method of this invention provides for an automated tissue type classification scheme. The results from a full spectral mapping of the optical reflectance and fluorescence radiation from test samples can be compared with standard libraries of comparable emission profiles from healthy and unhealthy tissues. Thus the spectral signature outputs from spectrometer are used as the input for comparison to a stored reference database. This could be done locally, or remotely using a central database connected to the Internet, for example.

To gain a better understanding of the invention described herein, the following examples are set forth. It should be understood that these examples are for illustrative purposes only. Therefore, they should not limit the scope of this invention in any way.

EXAMPLES

EXAMPLE I: SPECTROMETER INCORPORATING A MATCHED FILTER RECEIVER

One embodiment is shown in Figure 15 comprising a light source, for example, a miniature Xenon bulb that has an emission spectrum approximately equal to that of a

6000 °K Blackbody with a few discrete spectral lines. The light is collimated and modulated by a chopper wheel, which provides a 500 Hz On-Off modulation to the light entering the Illumination Monochromator. The Illumination Monochromator operating under the control of the CPU sweeps the illumination wavelength from 250 nm to 800 nm in steps of 10 nm. This illumination is focused onto the Area of Interest. The Emission Monochromator operating under the control of the CPU sweeps the illumination wavelength from 250 nm to 800 nm in steps of 10 nm. It is controlled in such a way that for every illumination wavelength sample λ_i, it sweeps over the range of wavelengths greater than or equal to λ_i. A Ga-As photodiode is used as the optical detector, with the signal from the photodiode being amplified by a Low Noise Amplifier (LNA). The output of the LNA can be filtered using an analog filter, or it can be digitized using an Analog to Digital Converter (ADC) and processed digitally using an IIR or FIR digital filter. The detector output is recorded for each λ_i and λ_e, and can be plotted for display as shown in Figure 16, which can allow easy comparison of samples of healthy tissue with those which are know to be abnormal.

One important issue to be dealt with is the magnitude versus wavelength calibration of the system, since the Xenon Light source is not spectrally flat. This can be done using a standard diffuse reflection source, which has spectrally flat in an optical wavelength sense. The calibration factor can then be applied to the collected data such that the spectral coloring of the illumination source can be removed from the data. This process is essentially spectral equalization of the data.

Once the data is equalized, it can be displayed in a number of ways such as contour plots, surface plots, etc. for easy visualization of the illumination/emission spectra. This may require some normalization to say the strongest spectral peak of some response at a fixed wavelength location. This will have to be determined experimentally. An example of a surface type of plot is shown in Figure 16. Once the data has been acquired, a database of healthy tissue types and unhealthy tissue types can be acquired. This database can be used as the bases of an automated or computer aided classification system using standard classification techniques. This could be used to identify suspect areas to a practitioner so

that they could give apply further techniques (not necessarily related to the spectrometer) to investigate the tissue.

EXAMPLE II

One embodiment of this invention comprises an optical system comprising a spectrometer, an electronic light modulator and digital signal processing means, including: a) a light emitting diode (LED), as the illumination light source, which is controlled by said digital signal processing means to emit a radiation bandwidth ranging from 380 to 500 nanometers; b) a stepper motor controlled, grating monochromator which is controlled by said digital signal processing means to receive light from the illumination device and to deliver the N^{th} wavelength in a pulse sequence; c) an optical fibre probe that is coupled to the monochromator with collimating and focusing elements that delivers the N^{th} wavelength to a subject area, located in an assembly that orients the illumination optics with that of the collecting optics such that they are at a constant angle to each other; d) collecting means for gathering the resultant radiation of the N^{th} wavelengths and delivering the information via light collection lenses and fibre coupled to the stepper motor controlled, grating detection monochromator; and e) a photodetector such as a Ga-As Integrated Photodiode and Amplifier. The stepper motor controlled, grating monochromators are controlled by said digital signal processing means to perform tasks to pass the N^{th} wavelength reactive characteristics at a specific time.

Typically a Ga-As Integrated Photodiode and Amplifier is made up of stock electronic components that consist of a photodiode and transimpedance amplifier on the same chip. This is sampled by the digital signal processing means to sense the radiation at a specific time. A photodiode is used as an optical detector, with the signal from the photodiode being amplified by a Low Noise Amplifier (LNA). The output of the LNA is filtered using an analog filter to condition the signal from the photodetector with an op amp amplifying the signal to a specific range and digitised using an Analog to Digital Converter (ADC) and processed digitally using an FIR digital filter and a digital signal

coding software technique such that a time/bandwidth product can be measured using a correlation receiver.

The system further comprises a DSPS device where an illumination modulation coding signal is created using a 32 bit linear FM pulse coding technique for pulse compression, the detection pulse coding is resolving the time bandwidth product with a matched correlation receiver, and the detection of specific amplitudes of irradiance can prompt the DSPS to run a specific routine to test for specific signal response characteristics in this case fluorescence and reflectance can be measured depending on the limitations of the wavelengths of illumination. The monochromator gratings can operate through the visible spectrum and can be substituted for other wavelengths into the UV or IR ; and a digital signal processing technique such that software that recognises the peaks of data and their rule based weighted relevance can control the illuminator and detector monochromators.

EXAMPLE III

In one embodiment of the present invention an optical system can be designed with the ability to control the wavelength of the scan (illumination radiation) including modulation techniques. This type of optical system can provide maximum optical flexibility in relation to research and diagnostic applications.

An embodiment of the optical system designed for this scenario comprises: a digital signal processing means which is integrated into a computing device with the emitter control electronics comprising pulse code software to create a synchronous pulse for direct modulation of the optical emission processing means frequency and the received signal processing means incorporating a signal correlation match filter; a flashlamp providing the photonic energy source; optical emission processing means incorporating a frequency modulator circuit for modulating the illumination radiation, a refractive or diffractive optical system whereby the optical centre wavelength is chosen by the use of a position controller to move the fixed light conditioning optics of the emitter optical

system; received light optical processing means incorporating a refractive or diffractive optical system whereby the optical centre wavelength is chosen by the use of a position controller to move the fixed light conditioning optics of the detector optical system; and a silicon APD photodetector acting as the optical detector.

EXAMPLE IV

In one embodiment of the present invention an optical system can be designed for maximum sensitivity of resultant radiation resulting from the illumination of a test sample by a known wavelength of light. This type of optical system can be useful for fluorescence analysis, especially if a spectral probe is attached to the subject of interest and has know spectral properties such that detection of a specific wavelength of fluorescence, absorption or reflection can be measured.

An embodiment of the optical system designed for this scenario comprises: a digital signal processing means which is integrated into a computing device with the emitter control electronics comprising pulse code software to create a synchronous pulse for direct modulation of the optical emission processing means frequency and the received signal processing means incorporating a signal correlation match filter; a laser providing the photonic energy source; optical emission processing means incorporating an acousto-optic scanner and a fixed emitter optical system; received light optical processing means incorporating fixed light conditioning optics; and a photomultiplier acting as the optical detector.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A system comprising a spectrometer, an electronic light modulator and digital signal processing means, including:
   (a) a photonic energy source which is controlled by said digital signal processing means to emit electromagnetic radiation ranging from ultraviolet to far infrared (or bandwidth from 150 to 3000 nm);
   (b) a monochromator which is controlled by said digital signal processing means to receive light from an illumination device and to deliver one or more wavelengths to an optical probe;
   (c) an optical probe, which delivers light at one or more wavelengths to a subject area, located in an assembly that orients the illumination optics with that of the collecting means for gathering and delivering the resultant radiation to the detection monochromator;
   (d) a monochromator source which is controlled by said digital signal processing means to perform specific digital signal processing tasks to pass the one or more wavelengths' reactive characteristics at a specific time;
   (e) a photodetector device which is controlled by said digital signal processing means to sense the radiation at a specific time; and
   (f) a digital signal processing means to perform the match filtering on the output of the photodetector.

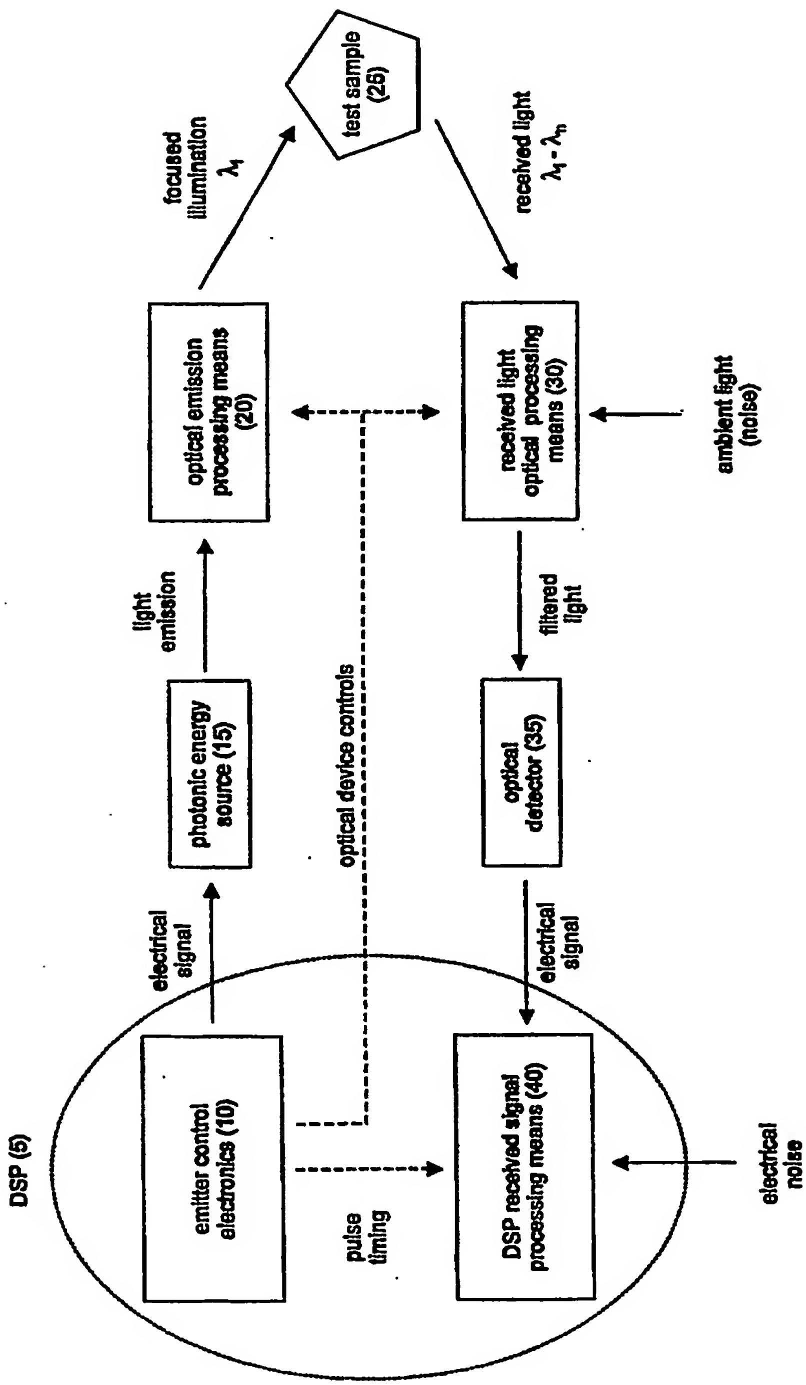

DSP (5)
emitter control electronics (10)
electrical signal
photonic energy source (15)
light emission
optical emission processing means (20)
focused illumination λ_1
test sample (25)
received light $\lambda_1 - \lambda_n$
received light optical processing means (30)
ambient light (noise)
filtered light
optical detector (35)
electrical signal
optical device controls
pulse timing
DSP received signal processing means (40)
electrical noise

FIGURE 1

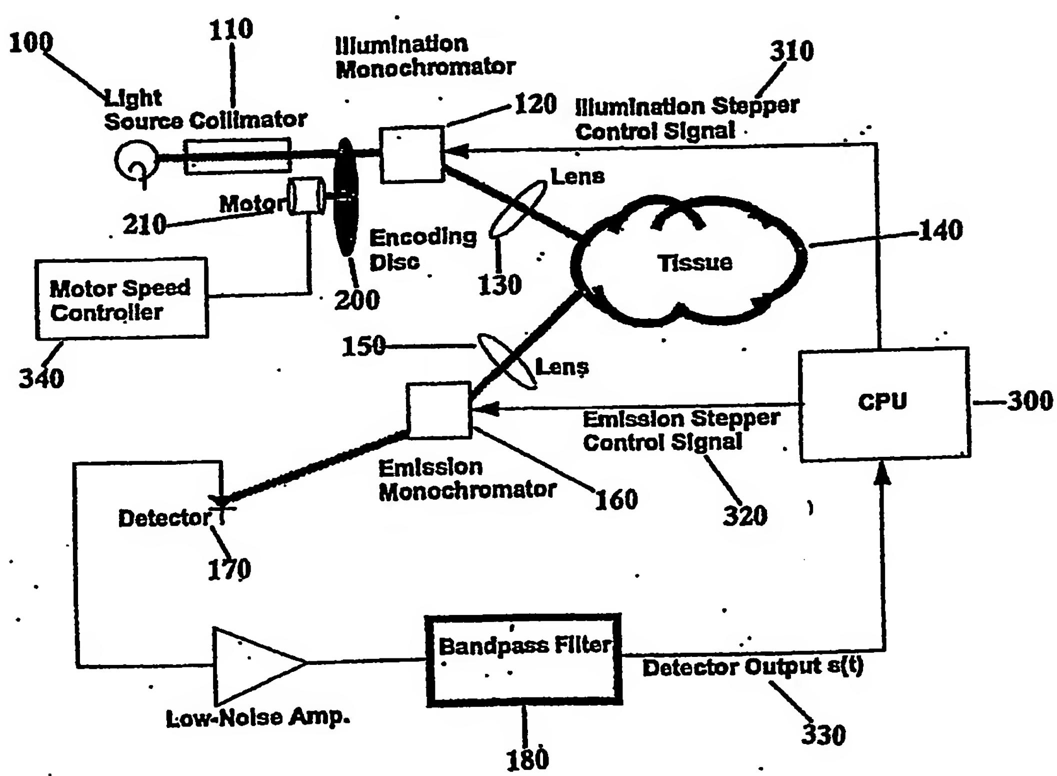

100
110
Illumination Monochromator
310
Light Source
Collimator
120
Illumination Stepper Control Signal
Lens
Motor
210
Encoding Disc
Tissue
140
Motor Speed Controller
200
130
150
Lens
340
CPU
300
Emission Stepper Control Signal
Detector
Emission Monochromator
160
320
170
Bandpass Filter
Detector Output s(t)
Low-Noise Amp.
180
330

FIGURE 2

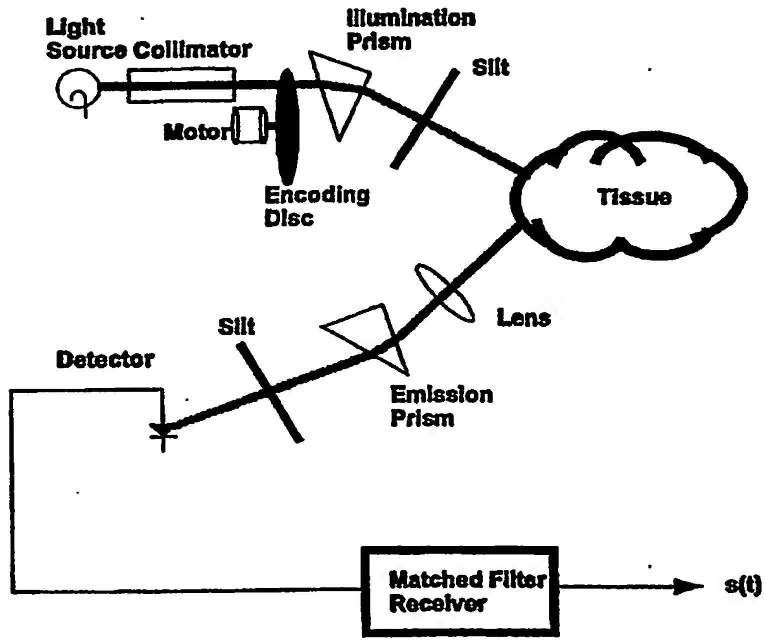

Light
Source
Collimator
Illumination
Prism
Slit
Motor
Encoding
Disc
Tissue
Lens
Slit
Detector
Emission
Prism
Matched Filter
Receiver
s(t)

FIGURE 3

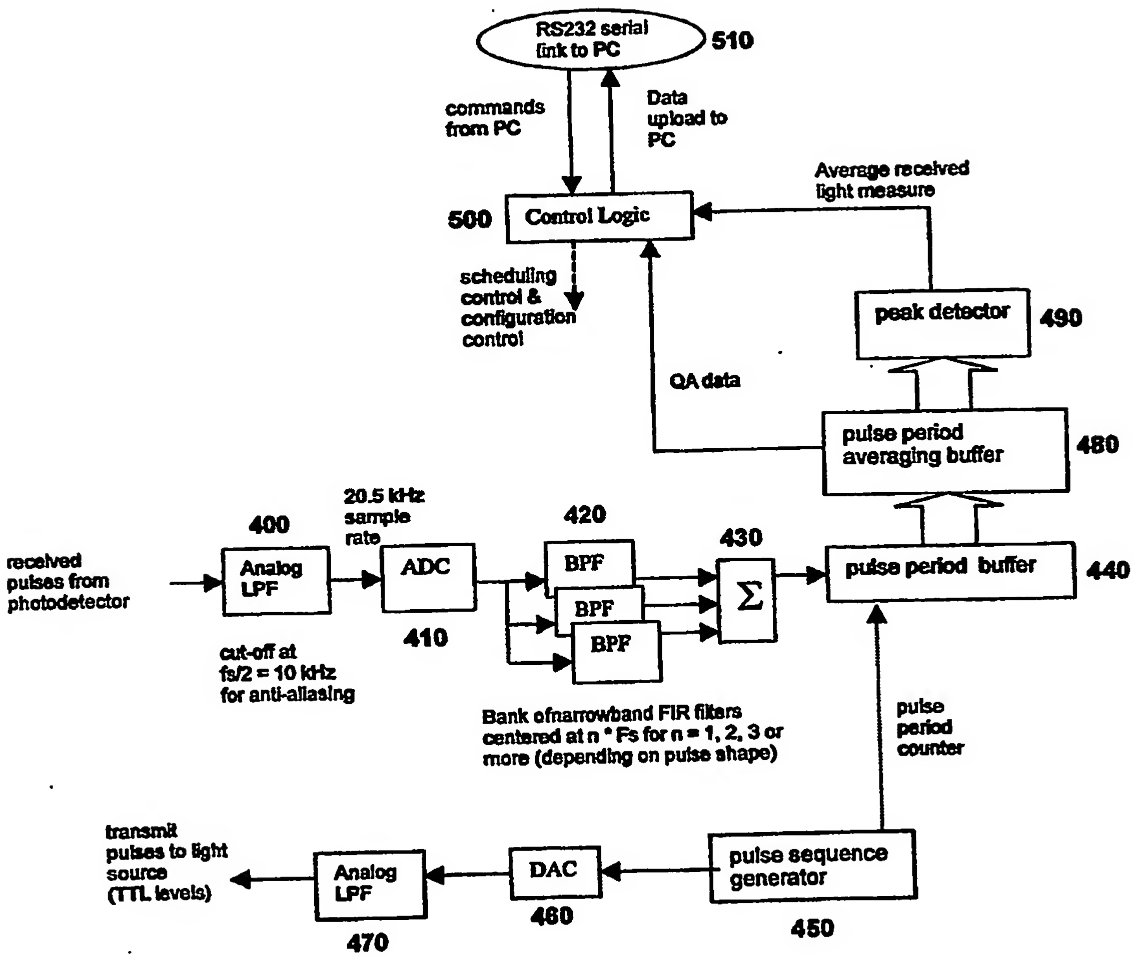

RS232 serial link to PC
510
commands from PC
Data upload to PC
Average received light measure
500
Control Logic
scheduling control & configuration control
peak detector
490
QA data
pulse period averaging buffer
480
20.5 kHz sample rate
400
420
430
received pulses from photodetector
Analog LPF
ADC
BPF
BPF
BPF
Σ
pulse period buffer
440
410
cut-off at fs/2 = 10 kHz for anti-aliasing
Bank of narrowband FIR filters centered at n * Fs for n = 1, 2, 3 or more (depending on pulse shape)
pulse period counter
transmit pulses to light source (TTL levels)
Analog LPF
DAC
pulse sequence generator
470
460
450

FIGURE 4

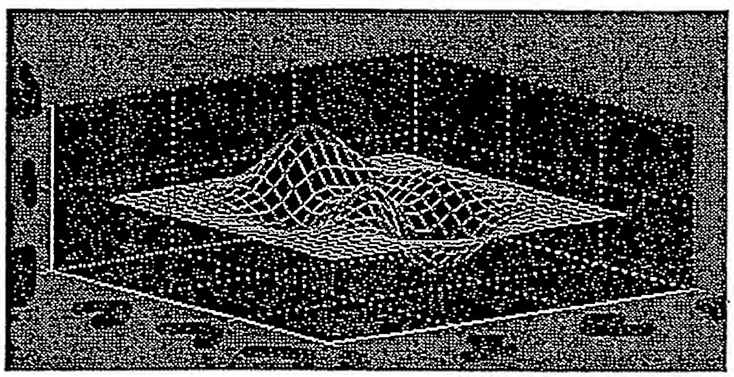


FIGURE 5

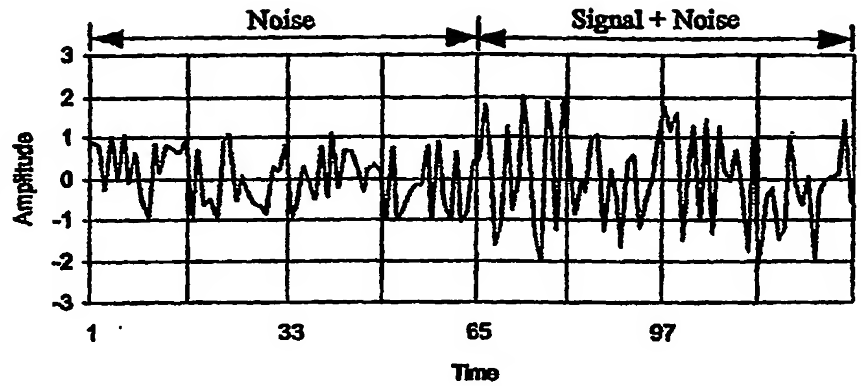


FIGURE 6

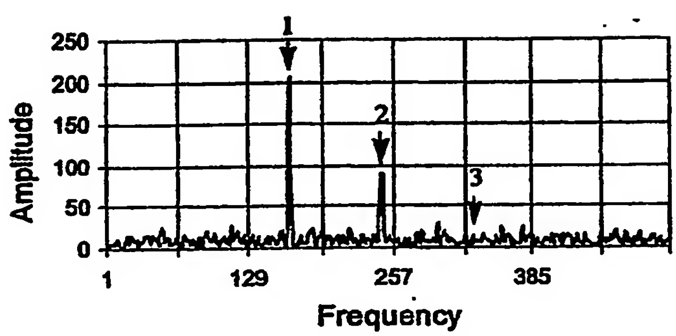


FIGURE 7

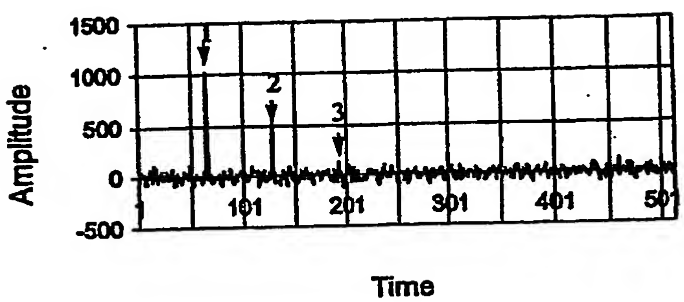


FIGURE 8

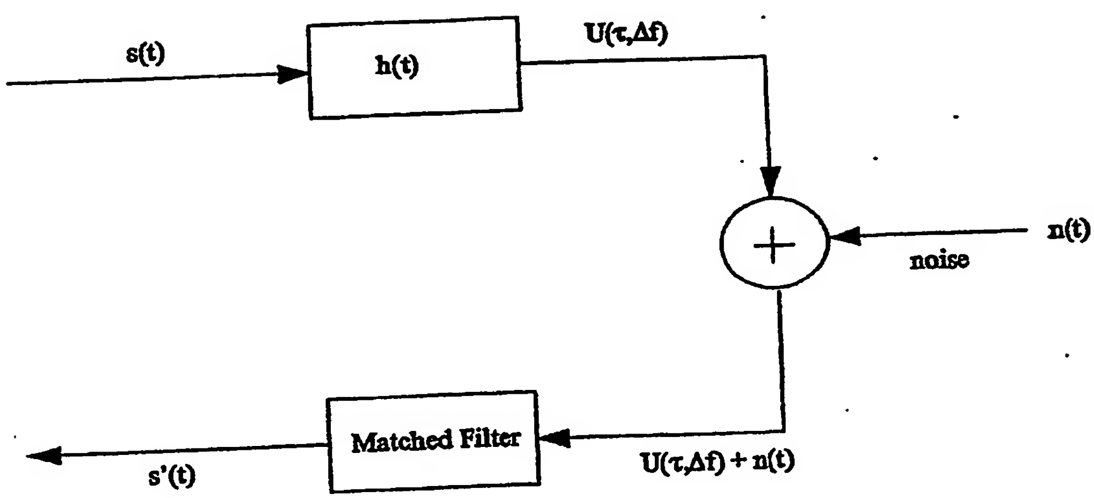


FIGURE 9

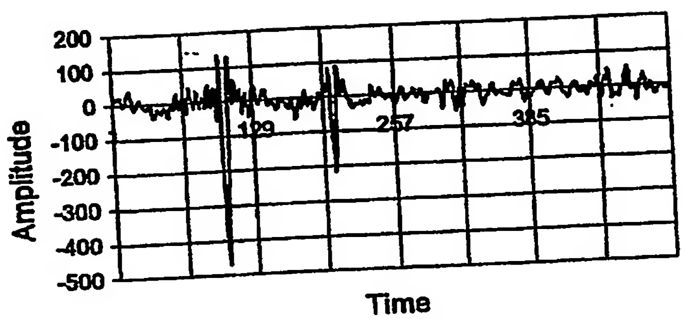


FIGURE 10

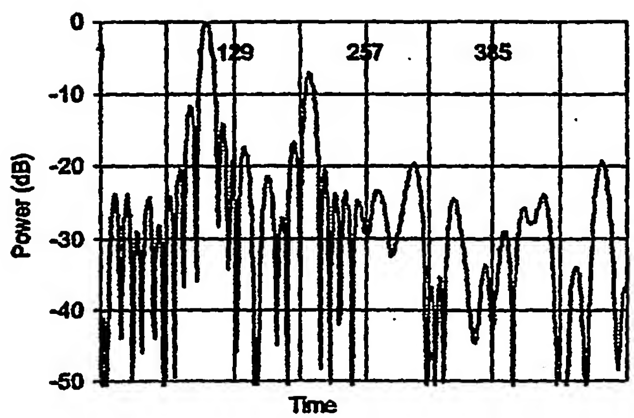


FIGURE 11

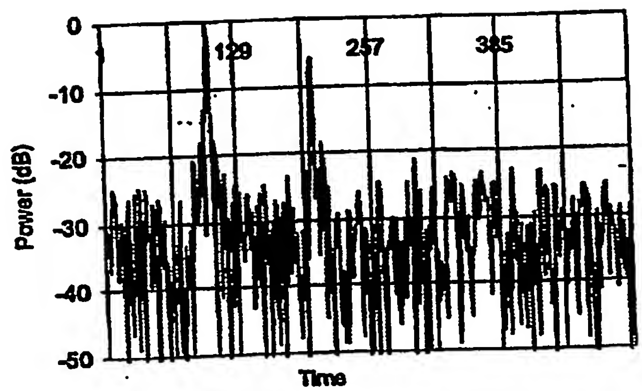


FIGURE 12

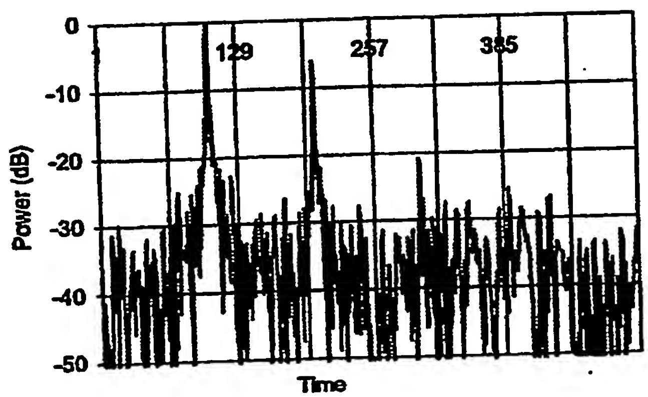


FIGURE 13

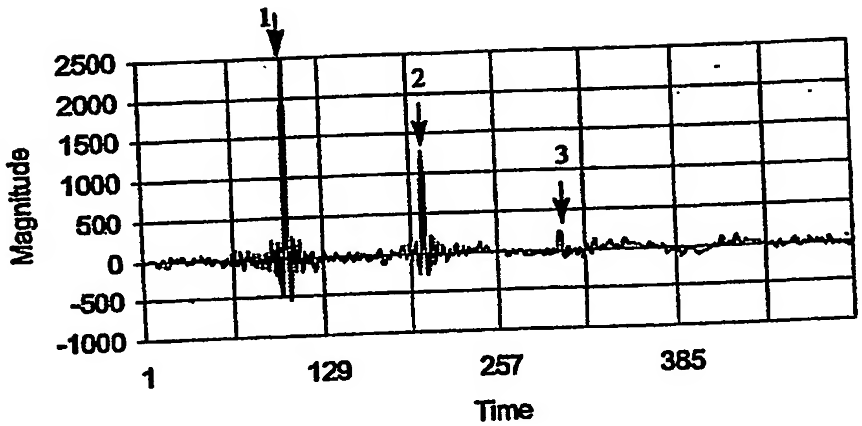
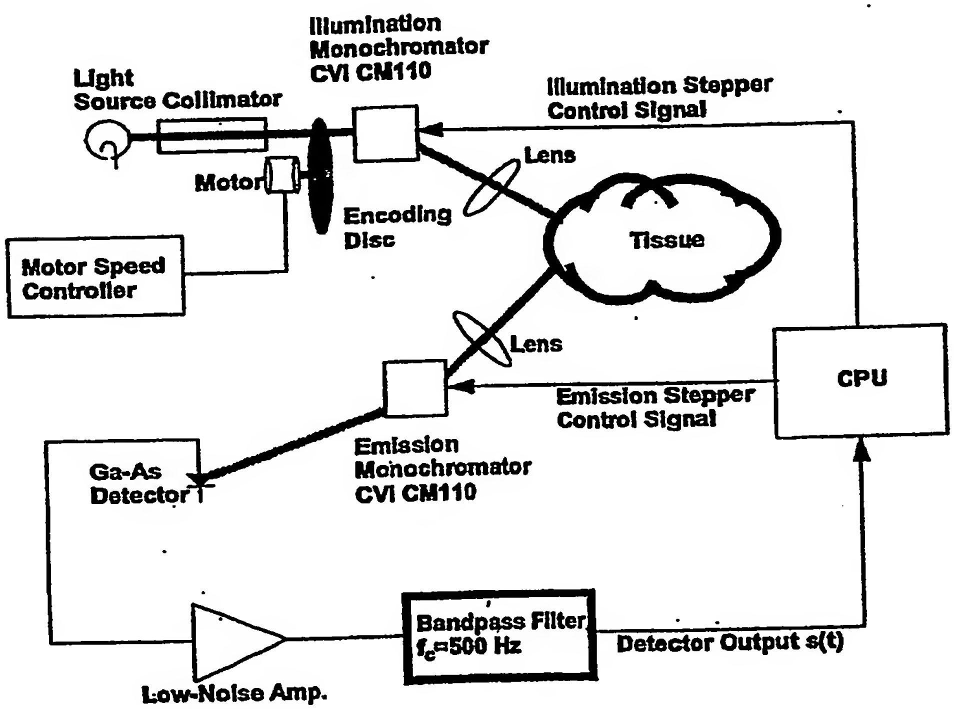
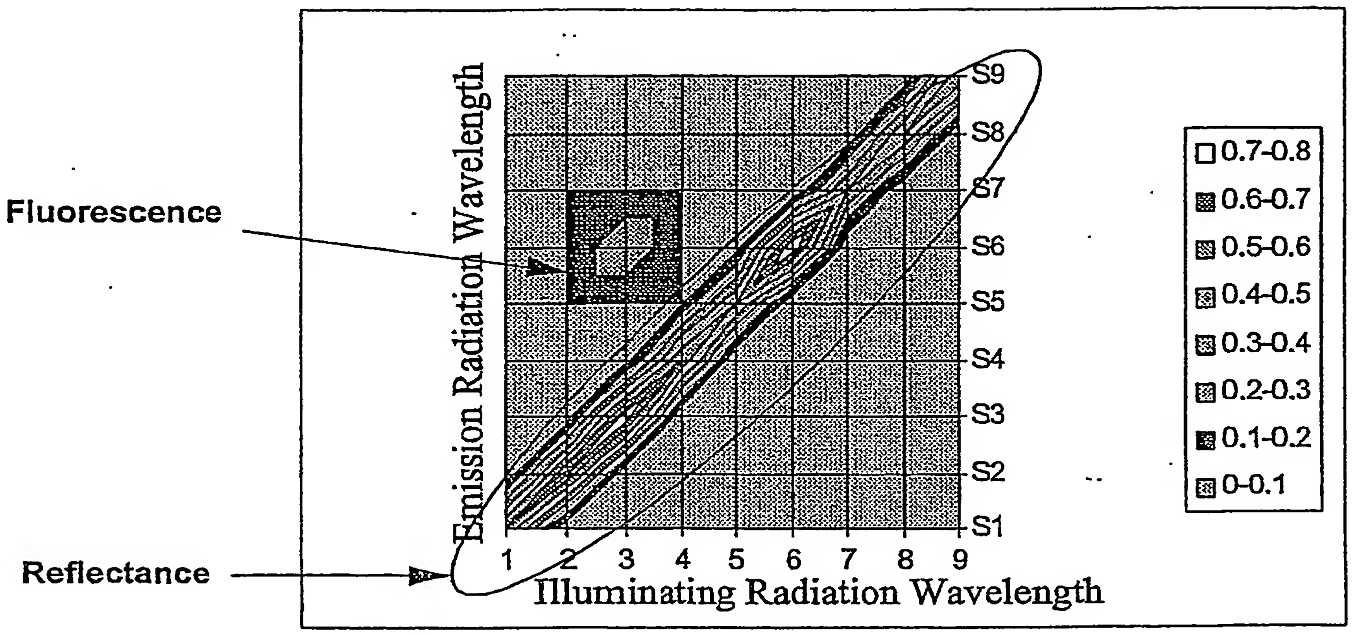

1
2
3
2500
2000
1500
1000
500
0
-500
-1000
Magnitude
1
129
257
385
Time

FIGURE 14



Illumination Monochromator CVI CM110
Light Source
Collimator
Illumination Stepper Control Signal
Lens
Motor
Encoding Disc
Tissue
Motor Speed Controller
Lens
CPU
Emission Stepper Control Signal
Ga-As Detector
Emission Monochromator CVI CM110
Bandpass Filter
f_c=500 Hz
Detector Output s(t)
Low-Noise Amp.

FIGURE 15



Fluorescence
Reflectance
Emission Radiation Wavelength
Illuminating Radiation Wavelength
1 2 3 4 5 6 7 8 9
S1 S2 S3 S4 S5 S6 S7 S8 S9
0.7-0.8
0.6-0.7
0.5-0.6
0.4-0.5
0.3-0.4
0.2-0.3
0.1-0.2
0-0.1

FIGURE 16